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THE INCREASING INCIDENCE OF EXTENDED-SPECTRUM BETA-LACTAMASE-PRODUCING STRAINS OF *ESCHERICHIA COLI* AND *KLEBSIELLA PNEUMONIAE*

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Purpose: The incidence of extended-spectrum beta-lactamase (ESBL)-producing strains of *Escherichia coli* and *Klebsiella pneumoniae* is increasing worldwide, which may change empiric antibiotic treatment. This study was conducted to explore the increasing extent of the incidence of ESBL-producing strains (ESBLPS) in *E. coli* and *K. pneumoniae*.
Methods: This was a retrospective study at a regional hospital in southern Taiwan. From 2009 to 2013, all *E. coli* and *K. pneumoniae* isolates from clinical microbiology laboratory were enrolled in this study. ESBLPS were confirmed by double disk diffusion test.
Results: A total of 15954 *E. coli* and 5374 *K. pneumoniae* isolates were enrolled. The ESBLPS accounted for 10.7% (325/3048) and 16.8% (186/1109), 12.1% (362/2989) and 16.1% (155/963), 13.3% (447/3359) and 19.2% (214/1112), 17.4% (633/3635) and 20.8% (219/1051), as well as 20.5 % (753/2923) and 20.2% (230/1139) of *E. coli* and *K. pneumoniae* isolates in 2009, 2010, 2011, 2012, and 2013, respectively. The incidence of ESBLPS of *E. coli* and *K. pneumoniae* was statistically significant difference between 2009 and 2013 ($P < 0.05$).
Conclusions: As a result of this study, the incidence of ESBLPS of *E. coli* and *K. pneumniae* was statistically significant increase from 2009 to 2013 (10.7% versus 20.5% in *E. coli* and 16.8% versus 20.2% in *K. pneumoniae*). The incidence of ESBLPS of *E. coli* was lower than that of *K. pneumoniae* before 2012, but that was similar in 2013. We think that the rapid increase of ESBLPS of *E. coli* should be concerned in clinical practice because *E. coli* is more frequent organism causing infections than *K. pneumoniae*.

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REPORT AN ISOLATE OF IMIPENEM-RESISTANT *PROTEUS MIRABILIS*

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Purpose: To report an isolate of imipenem-resistant *Protues mirabilis* and investigate the cause of resistance to imipenem.
Methods: An isolate of *P. mirabilis* was isolated from urine of a patient lived at nursing home. Disk diffusion testing was used for antimicrobial susceptibility testing and E-test was used to determine the minimal inhibitory concentation (MIC) of imipenem. The results were interpreted according to the criteria recommended by the Clinical Laboratory Standards Institute 2014. Polymerase chain reaction (PCR) and sequencing were used to detect â-lactamase, including carbapenemase, and porin mutation.
Results: Antimicrobial susceptibility testing revealed the isolate was resistant to cefazolin, cefuroxime, cefoxitin, ceftriaxone, ceftazidime, ampicillin-sulbactam, piperacillin-tazobactam, gentamicin, amikacin, levofloxacin, trimethorpim-sulfamethoxazole, and imipenem; and sensitive to cefepime, ertapenem, and meropenem. The MIC of imipenem was >32 μg/ml. PCR and sequencing revealed only bla_{CMY-2} was detected and some mutation of ompF was present.
Conclusions: As a result of this study, the cause of the *P. mirabilis* resistant to â-lactams except cefepime and carbapenems was producing of CMY-2 â-lactamase, and resistant to imipenem was producing CMY-2 â-lactamase combined with porin deficiency. We think imipenem-resistant *P. mirabilis* is worthy of attention. If it is also resistant to other carbapenems, it may become pandrug-resistant organism because *P. mirabilis* is intrinsically resistant to the two last resort antibiotics, namely tigecycline and colistin.

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EVALUATE THE SENSITIVITY AND SPECIFICITY OF DETECTING CARBAPENEM-RESISTANT *ENTEROBACTERICEAE* BY ERTAPENEM

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Purpose: According to the definition of the U.S. Centers for Disease Control and Prevention, carbapenem-resistant enterobactericeace (CRE) are defined as enterobactericeae that are nonsusceptible to imipenem, meropenem, or doripenem; and resistant to third-generation cephalosporins, including cefotaxime, ceftriaxone, and ceftazidime. For *Proteus* spp., *Providencia* spp., and *Morganella morgannii*, those must be also nonsusceptible to other carbapenems except imipenem. Ertapenem is known as the most sensitive antibiotic for detecting CRE, but the specificity is low. This study was conducted to evaluate the extent of the sensitivity and specificity of detecting CRE by ertapenem alone.
Methods: At a regional hospital, from September 2013 to August 2014, all enterobactericeae nonsusceptible to one of carbapenems (including ertapenem, imipenem, meropenem, and doripenem) were enrolled in this study. In those isolates, if they fulfilled the above-mentioned criteria, they were defined as CRE.
Results: A total of 103 isolates, including 38 CRE and 65 non-CRE, were enrolled. Of all CRE, 37 were resistant to ertapenem and one was susceptible to ertapenem. Of all non-CRE, 53 were resistant to ertapenem and 12 were susceptible to ertapenem. The sensitivity and specificity of detecting CRE by ertapenem alone was 97.4% (37 of 38) and 18.5% (12 of 65), respectively.
Conclusions: As a result of this study, ertapenem alone had 97.4% sensitiviity of detecting CRE, but only had 18.5% specificity. Accordingly, If CRE are defined as enterobactericeae that are nonsusceptible to ertapenem alone, which will have an overestimate of CRE up to 81.5%.

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IN-VITRO ACTIVITIES OF COMBINATION BETWEEN TIGECYCLINE, COLISTIN, AND FOSFOMYCIN AGAINST *KLEBSIELLA PNEUMONIAE* (KP) ISOLATES WITH EXTENDED-SPECTRUM β-LACTAMASE (ESBL) PHENOTYPE

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Purpose: The emergence of carbapenem-resistant Enterobacteriaceae has severely limited the option of antimicrobial therapy against ESBL-producers. We aimed to evaluate the potentially alternative antimicrobial strategy for treating infections caused by ESBL-producing KP isolates using non-carbapenem regimens.
Material and methods: We investigated the synergism between any two of tigecycline, colistin and fosfomycin against 6 clinical isolates of ESBL-KP strains (designed KP 357, 402, 403, 420, 324, 441) from patients hospitalized in a medical center in southern Taiwan. Synergism was evaluated by time-kill studies. The in-vitro activities of tigecycline, colistin and fosfomycin was tested by using 1/2 x MIC and 1/4 x MIC for each drug concentration alone or for any two drugs. The standard inoculum of bacterial densities was a suspension containing 5×10^5 CFU/mL. Bactericidal activity was defined as a ≧ 3-$\log_{10}$ CFU/mL decrease at least lasting for 24 hours in viable cell counts compared to the original inoculum. Synergistic effect was defined as ≧ 3-$\log_{10}$ CFU/mL compared to the most active drug.
Results: Only 2 strains (KP 357 and 441) reached synergistic effects by 1/2 MIC of tigecycline plus fosfomycin. Only 2 strains (KP 403 and 423) reached synergistic effects by 1/2 MIC of colistin plus fosfomycin. All 6 isolates reached synergistic effects by 1/2 MIC of tigecycline plus colistin, and even 4 strains (KP 357, 410, 423 and 441) reached synergistic effects by 1/4 MIC of tigecycline plus colistin.
Conclusions: The combination activity of tigecycline and colistin showed the most in-vitro synergistic effects against the tested ESBL-KP isolates.

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CEFEPIME THERAPY FOR URINARY TRACT INFECTIONS CAUSED BY EXTENDED-SPECTRUM β-LACTAMASES (ESBLS)-PRODUCING *ESCHERICHIA COLI*: FROM EX VIVO MODEL OF URINARY BACTERICIDAL ACTIVITY TO CLINICAL APPLICATION

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Background and purpose: The clinical role of cefepime therapy for urinary tract infections (UTIs) caused by so called susceptible Extended-Spectrum β-Lactamases (ESBL)-producing *Escherichia coli* remains unclear. The aim of this investigation was to assess the urinary bactericidal activity of cefepime against ESBL-producing *E. coli* isolates in ex vivo model.